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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,654	10/24/2003	Tomoko Maeda	244295US0CONT	1300

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EXAMINER

AFREMOVA, VERA

ART UNIT PAPER NUMBER

1651

DATE MAILED: 09/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,654	MAEDA ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21,22 and 26-44 is/are pending in the application.
- 4a) Of the above claim(s) 26-44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21,22 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152..

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION***Election/Restrictions***

Applicant's election with traverse of the Group I, claims 21, 22 and 25, in the reply filed on 6/06/2006 is acknowledged. The traversal is on the ground(s) that the claimed methods are not materially different and there is no serious burden in searching and examining all groups of claims. This is not found persuasive because the presently claimed methods having different scope as claimed and, thus, the references that would be applied to one group of claims would not necessarily anticipate or render obvious the other group(s). Moreover, as to the question of burden of search, classification of subject matter is also an indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exists. Clearly different searches and issues are involved with each group. For these reasons, the restriction requirement is deemed proper and is adhered to. The restriction requirement is hereby made FINAL.

Claims 42-44 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected groups of inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on 6/06/2006.

Claims 1-20, 23, 24 were canceled by applicants.

Claims 26-41 remain withdrawn from examination as drawn to non-elected inventions.

Claims 21, 22 and 25 are under examination in the instant office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 21, 22 and 25 rejected under 35 U.S.C. 102(a) as being anticipated by Khalkhali-Ellis et al. ("Expression of macrophage markers by a population of cells obtained from synovial fluid of a subgroup of patients with juvenile rheumatoid arthritis". The Journal of Rheumatology. February 1998, Vol. 25, No. 2, pages 352-360).

Claims are directed to a method for producing osteoclast precursor cells wherein the method comprises steps of obtaining cells in a cellular fraction containing granulocytes and lymphocytes from joint fluid by centrifugation culturing the cells in an essential medium for mammalian cells with added serum and in the absence of any additional cytokine(s). Some claims are further drawn to culturing the cells at temperature ranging from 35-37°C in 5-7% CO₂ containing air for 1-3 weeks.

The cited reference by Khalkhali-Ellis et al. discloses a method for culturing cells derived from synovial or joint fluid of patients with rheumatoid arthritis wherein the method comprises steps of obtaining mononuclear cell population from joint fluid by centrifugation and culturing the cells in RPMI essential medium for mammalian cells with 10% serum and in the absence of any additional cytokines. The cells are cultured at 35°C in 5 % CO₂ containing air for 1-3 weeks (page 353, col. 2, par. 2). The mononuclear cell population isolated from synovial fluid by

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centrifugation is a mixed cell population that contains macrophages, granulocytes and lymphocytes and, thus, the same starting cell population as claimed and when read in the light of specification (page 12). The cited method comprises identical active step(s) of culturing identical cell population under identical culture conditions for identical period of time, and, thus, the final result is reasonably considered to be identical as intended for the claimed method.

Thus, the cited reference by Khalkhali-Ellis et al. is considered to anticipate the claimed invention.

2. Claims 21,22 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Fujikawa et al. ("Human osteoclast formation and bone resorption by monocytes and synovial macrophages in rheumatoid arthritis". *Annals of Rheumatic Diseases*. 1996. Vol. 55, pages 816-822).

Claims as above.

The cited reference by Fujikawa et al. discloses a method for producing osteoclast precursor cells wherein the method comprises steps of obtaining cells from synovial tissue by centrifugation (page 817, col. 1, last par.) and culturing the cells in MEM (minimal essential medium) for mammalian cells with added serum and in the absence of any additional cytokines (page 817, col.2, par. 3) for at least 1 week (page 819, col. 1, par. 2, lines 12-17). Although the cited reference appears to be silent about temperature and air conditions, the claimed conditions are regular mammalian cell culture requirements. Moreover, the cells from synovial fluid were handled at temperature within the range 35-37°C (page 817, col. 1 , last par.) and 5-7% CO₂

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containing air is regular atmosphere. The cited method comprises identical active step(s) and identical structural elements as required by the claimed method.

Thus, the cited reference by Fujikawa et al. is considered to anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 21, 22 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Khalkhali-Ellis et al. ("Expression of macrophage markers by a population of cells obtained from synovial fluid of a subgroup of patients with juvenile rheumatoid arthritis". The Journal of Rheumatology. February 1998, Vol. 25, No. 2, pages 352-360) and Fujikawa et al. ("Human osteoclast formation and bone resorption by monocytes and synovial macrophages in rheumatoid arthritis". Annals of Rheumatic Diseases. 1996. Vol. 55, pages 816-822).

Claims are above.

The cited references by Khalkhali-Ellis et al. and by Fujikawa et al. are relied upon as explained above for the disclosure of methods of culturing cells isolated from synovial tissue including synovial fluids wherein the same starting cell populations are cultured under the same conditions for the same time periods as required by the claimed method. Although the cited reference by Khalkhali-Ellis et al. is silent about the preosteoclast/osteoclast nature of cells in the

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final cell mixture, the reference by Fujikawa et al. explicitly teaches that the synovial mononuclear cells demonstrate development towards preosteoclast and osteoclast cells.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to culture monocytes from synovial fluid with a reasonable expectation of success in producing preosteoclast cells as adequately demonstrated by the cited references. One of skill in the art would have been motivated to obtain and/or to culture preosteoclast cells from synovial fluid for the expected benefits in determining mechanism for pathogenesis of bone destruction in the context of inflammatory disease such as rheumatoid arthritis.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

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September 15, 2006

A handwritten signature in black ink, appearing to read 'V. Afremova', with a long horizontal flourish extending to the right.

VERA AFREMOVA

PRIMARY EXAMINER